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10/087,715	03/01/2002	Kathleen S. Keegan	27866/37081A/US	7406
4743	7590	12/19/2003	EXAMINER	
MARSHALL, GERSTEIN & BORUN LLP 6300 SEARS TOWER 233 S. WACKER DRIVE CHICAGO, IL 60606			PATEL, SUDHAKER B	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/087,715

**Applicant(s)**

KEEGAN ET AL.

**Examiner**

Sudhaker B. Patel, D.Sc.Tech.

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 1 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7/1/02. 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of invention of Group I in Paper dated 11/03/03 is acknowledged. The traversal is on the ground(s) that the subject matter is the same for the different inventions, and search for claims 1-31 would not be a serious burden on the examiner. This is not found persuasive because of the reasons already stated in earlier office communication dated 9/5/03. Additionally, the components W & Z as recited in generic Formula of claim 1 ( $=W-X1-C(=y)-X2-Z$ ), simultaneously represent multiples of combinations with different meaning of the bridge  $(=X1-C(=y)-X2-$ . E.g. (1). Heteroaryl-bridge-Heteroaryl.(2).Aryl-Bridge-Hydro.(3).Aryl-Bridge-Aryl.(4).Aryl-bridge-Heteroaryl.(5).Heterocycloalkyl-Bridge-Z.(6).Cycloalkyl-Bridge-Z.(7).C1-3alkyl substituted with heteroaryl-Bridge-Z and others. The meanings of bridge  $-X1-C(=y)-X2-$  as recited will produce among many, a few bridges e.g. (1)  $-CH_2-NH-$ .(2).  $-CH_2-O-$  .(3).  $-CH_2-S-$  .(4).  $-NH-CO-NH-$  .(5).  $-NH-CS-NH-$  .(6).  $-NH-CH_2-NH-$  .(7).  $-O-CH_2-O-$  .(8).  $-S-CH_2-S-$  . Therefore, as already stated earlier , the inventions are distinct, each from the other because of the following reasons:

- (1). The compounds of Groups I-II are drawn to structurally dissimilar Chemicals.
- (2). The compounds are made and used independently of each other.
- (3). They would be expected to raise different issues of patentability if a 1,4-diazine-Bridge-Phenyl compound of Group I was anticipated by Group II, the anticipatory reference would not necessarily render obvious the compounds of Group II or vice-versa.
- (4). The Compounds are not art-recognized equivalents.
- (5). The Compounds are separately subclassified according to U. S. Patent Classification system
- (6). The Classes/subclasses will require separate burdensome searches both in the literature and computer databases.
- (7). The groups lack unity of invention (see MPEP 803.02).

Based on above stated data i.e. (1) - (7), claim 1 also lacks unity of invention.

The search for Pyrazine and CHK1 provided 2779722 hits. The search for Pyrazine and urea provided 1897 hits. The search for pyrazine and carboxamide provides 858 hits. Furthermore, the search for 1,4-diazine core classified in class 544, subclass 336 provided 951 hits. The utility class 514 for 1,4-diazine provided subclasses 183,252, 255 provided 1929, 2703,2880 hits respectively. Therefore the

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total hits for 1,4-diazine-urea-phenyl core alone, are more than 8000, and this would be in addition to search for Pyrazine-CHK1 group hits as stated above.

The preliminary search for compounds with other combination than invention of Group I provides following hits: (I). 1,2-oxazine has 331 hits. (II). 1,3-oxazine has 265 hits. (III). 1,4-oxazine has 165 hits. (IV). Morpholine has 656 hits. (V). 1,2,4-triazine has 201 hits. (VI). 1,2-diazine has 802 hits. (VII). 1,3-diazine has 838 hits. (VIII). Quinoxaline has 898 hits. Therefore, although the compounds of (I)-(VIII) fall in main class 544, their subclasses will generate additional more than 2500 hits as stated earlier. The utility class 514 with inflammation and cancer(s) will generate more hits for the search.

It is this search and examination which is time consuming and burdensome for additional compounds which are included in the definition of W-Bridge-Z components forming chemically different compounds. Examiner has searched invention of Group I with the structures of the species and claims 28 only within the time allotted for a thorough and complete search for a single application.

It is noted that applicants have provided a single species related to working examples 284, 285, 287, 289, in addition to species of claims 28, 29 of the specification.

Applicants have elected invention of Group I, and the species as recited above, involve Claims (in part) 1-6, 8-31, drawn to compounds of Formula (I), compositions and a method of use for the same.

Applicants are reminded of the election of species guidelines provided in MPEP 803.02, which are followed for the examination.

The elected species of compound of Examples 284, 285, 287, 289 as stated earlier has following meanings for variables in the generic Formula (I) of claim 1:

W (=unsubstantiated)	= Monocyclic, 6-membered unsaturated 1,4-diazine core;
Z	= Phenyl (= Aryl) substituted by -O-Sub, R27, R28;
Sub	= Alkaline-substituted piperidine;
X1	= -NH-;
-C (=y)-	= -CO-;
X2	= -NH-;
R27/R28	= H.

Initial search with above definitions of the variables, prior art was not found for the elected Examples. Therefore, search was expanded to the species of the invention of Group I, wherein Sub = Alkyl; R27 = H or alkyl or -CO-NH-alkaline-Pyridine and R28 as recited in claim 28 and no prior art(s) were located. Therefore, the search was expanded to the rest of the species of the entire Group I invention.

Since claims 1-6,8-31 link with other invention(s), they will be examined bearing in mind the subject matter and species as elected by applicants and restriction as stated above. Claim 7 is withdrawn from further consideration. Also, all other definitions than stated above for W & Z components are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected subject matter. See allowable subject matter below).

Additionally, there do exist prior art(s) for the compounds with Pyridine-Urea-pyridine (see Chemical Abstract DN 125:114487, also cited as WO 9611930); Phenyl-CO-NH-Phenyl (See Chemical Abstract DN 131:58657, also cited as WO9932433). This will raise additional issues related to rejections under either 35 U.S.C. 102(b) and 103(a).

Examiner appreciates applicants' IDS papers.

This application consists of more than 1 invention, and any additional thorough search for the rest of the subject matter than stated earlier would involve more time, which is burdensome to examiner.

The restriction/election requirement is still deemed proper, is maintained, and is therefore now made FINAL.

### ***Information Disclosure Statement***

1. The information disclosure statement (IDS) submitted on 7/1/02 is being considered by the examiner. Signed copy of the PTO Form 1449 is enclosed with this communication for applicants' record.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1,8,19,28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A). Claims 1,8,19,28-30 (where applicable) recites variable W as heteroaryl, aryl, heterocycloalkyl, C1-3alkylene substituted with a heteroaryl or aryl. These groups can be optionally substituted (where applicable) with one to 4 substituents which involve R3 component which also consists of aryl, heteroaryl, C1-6 alkyl substituted with one or more aryl, heteroaryl, heterocycloalkyl, alkyleneheteroaryl, heterocycloalkyl or two of R3 groups are taken together to form optionally substituted 3 to 6 membered aliphatic ring. The claims remain silent about the exact ring size; number of either carbon or heteroatoms(s) and their exact make up, and exact connecting point with carbon of main core. The term "one or more" does not say what is excluded from the claim(s). In re Sus et al., 135 USPQ 301 ; In re Lund et al., 153 USPQ 625. Correction is required with the exactly made compounds of Group I from the specification.

(B). Claim 1 and claims related to this claim, recite method of use recite: " a step of contacting the cell with an effective amount of a compound". Correction to: " a step of contacting the cell with a therapeutic effective amount of a compound" is required.

( C ). Claims 1, 8,19 recite:" a compound and pharmaceutically acceptable salts, prodrugs, or solvates thereof". Correction to:" a compound or pharmaceutically acceptable salts or prodrugs or solvates thereof" is required.

(D). Claim 19 recites components W' and Y' with different scope than main claim 1 which does not define W' and Z', and has also a term " solvates". Correction(s) is required.

(E). Claim 8 recite:" treatment of a medical condition by chemotherapeutic or radioisotherapeutic". The claim remains silent about the condition(s), and specific radiotherapy as well as the specific chemotherapeutic treatment, does not exactly say what is excluded. Correction is required.

(F). Claim 14 recites:" chemotherapeutic agent is selected from the group consisting of and alkylating agent, an antimetabolite, a hormone or antagonist thereof, a radioisotope, an antibody, and mixtures thereof". Claim remains silent about what is excluded from such terms. Correction is required.

### ***Claim Objections***

4. Applicant is advised that should claims 1, 8 be found allowable, claims 26, 27 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-18, 26, 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating rheumatoid arthritis, does not reasonably provide enablement for treating cancer(s) and other conditions related to inflammation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification and claims define various conditions and diseases in addition to arthritis, myeloid and round cell carcinoma, metastatic cancer, a cancer metastase, multiple myeloma, acute lymphocytic and non-lymphocytic leukemia, thymic lymphoma lung cancer, cancer of the adrenal cortex, small cell carcinoma, stomach-, colon-, breast, pancreatic-, liver-, bladder-, prostate-, testicular-, brain-, vaginal-, vulva-, ovarian-, squamous cell-, thyroid-, gall bladder-cancer(s), metastatic tumor cell invasion in the CNS, and conditions and diseases yet to be discovered.

7. In cases directed to chemical compounds, which are being used for their physiological/biological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See *in re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group and *In re Wiggins* 179 USPQ 421.

8. "Prodrug, Hydrate, Solvate and pharmaceutical Salts" as recited in the claims reads on all such moieties regardless of complexity of structure and point of attachment



to the aliphatic or carbocyclic or aromatic or heterocyclic core or bridge/chain for which there is no sufficient teaching how to make and how to use at any one selective location among the many possible sites present. The situation is more confusing when a skilled person in the art tries to visualize the multiple possibilities of combining a compound of claim 1 (or claims dependent on it) and/ or its composition in its " prodrug or solvate or salt form". Applicants provide no reasonable assurance that any and all derivatives of the instant compounds and their combinations either alone or in a combination therapy as outlined, will have ability to generate the compounds in vivo or in vitro by one or more processes.

9. In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ 2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include: (1). The nature of invention; (2). the state of prior art ; (3). the predictability or lack thereof in the art; (4). the amount of direction or guidance present; (5). the presence or absence of working examples; (6). the breadth of the claims, and (7). the quantity of experimentation needed.

Discussion about cancer(s):

10. For example, the claim sets forth not only for the treating brain cancer but also for treating of cancers related to ovaries, colon, prostate, inflammation, restenosis, and diseases yet not discovered generally. However, there never has been a compound capable of treating various types of cancers. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancers and pain as recited earlier, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in

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oncology. Even the most broadly effective anti-cancer agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities.

Thus, it is beyond the skill of oncologist today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task. This is only for one of the many disorders as claimed herein.

**Following references are quoted to show the state of art cancer:**

- ***Cecil Textbook of Medicine*** states that: " each specific type of cancer has unique biological and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see In re Butting, 163, USPQ 689 (CCPA 1969), wherein "evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers".
- **Structure-Based Design of Novel Anticancer Agent:**

Uckun et al(see Current Cancer Drug Targets, 1,59-71(2001) concludes in pages 66-67 that : " WHI-P131, which inhibits JAK3 but does not inhibit JAK1, JAK2, SYK,BTK,LYN or IRP even at concentrations as high as 350uM is undergoing further studies to evaluate its potential use as a new anti leukemic agent(in children). Agents that inhibit epidermal growth factor receptor(EGFR) may be useful for treatment of breast cancer. Tubulin modulating agents, which are of natural as well as synthetic origin, can be used as effective anticancer agents for treating breast cancer. COBRA compounds caused destruction of microtubule organization and apoptosis. Like other microtubule-interfering agents, COBRA compounds activated the proapoptotic c-Jun N-terminal kinase (JNK) signal transduction pathway, as evidenced by rapid induction of c-jun expression".

**Discussion about inflammation:**

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11. Enablement for the scope of "inflammatory diseases" generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, assorted leukotrienes and cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages, which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters.

Otitis media is an inflammation of the lining of the middle ear and is commonly caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. Cystitis is an inflammation of bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulites is inflammation of the tissues around eye, and Orbital cellulites is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics.

**Discussion about non-steroidal anti-inflammatory agents:**

Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of the causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally.

**Following references are cited to show the state of art for CHK1 and related subject matter(s):**

■ **Drug discovery targeting CHK1 and CHK2 kinases:**

Zhou et al(PubMed Abstract 14593735, also cited as Prog. Cell Cycle res., 5,413-21(2003)) state that:" Drugs targeting CHK1 and CHK2 have the potential to significantly improve the therapewutic window of DNA damaging agents available in the clinic". Thus, the instant compounds have not gone thru' various testing for the their utility as claimed herein.

■ **State of Differential response of human acute myeloid leukemia cells to known agents in vitro:**

Amica et al(PubMed Abstract 12576328, also cited as Blood, 101/11,4589-97(2003)) state that:" Our results suggest that the different molecular pathways induces by the drug in vitro may reflect, at least in part, the variable response to Gemtuzumab ozofofamicin(GO) obtained in vivo".

■ **CHK1-deficient tumor cells are viable but exhibit multiple checkpoint and survival defects:**

Zachos et al(PubMed Abstract 12554671, also cited as EMBO J. 22/3,713-23(2003)) state that:"Thus, CHK1 is dispensible for normal cell division in somatic DT40 cells but is essential for DNA damage-induced G(2)/M arrest and a subset of replication check point responses. Furthermore, CHK1-dependent processes promote tumor cell survival after perturbations of DNA structure or metabolism".

■ **Increase in termosensitivity of tumor cell by lowering intracellular pH:**

Song et al(PunMed Abstract 8384080, also cited as Cancer res. 53/7,1599-601(1993)) state that:" Our results strongly suggested that a combination of 1-

homopiperidyl-N-(diaminomethylene)pyrazine-carboxamide(HMA) and B-3(+) may preferentially thermosensitize tumors in vivo since the interstitial environment in tumors is acidic relative to that in normal tissues".

Specification on pages 203-212 recite various tests and assay methods for inhibition activity related to CHK1.

On page 206, applicants recite the results as: "All inhibitors tested were showed at least 5-fold selectivity for CHK1 over the other enzymes".

Applicants have not provided specifics related to detailed results for the species' activities recited herein. Therefore, comparison among the compounds cannot be made with the art-recognized ref. Compounds.

Such results and assays will only serve for the preliminary screening of many compounds, and not for treating the diseases as claimed herein.

The facts as provided above do support the need for additional quantity of experimentation, which would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the method of treatment for various disorders/conditions related to inflammation as well as cancer.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of instant compounds to control or prevent disorders related to inflammation

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006.

### **Conclusion**

### **Allowable Subject Matter**

12. Claims 19-25, 28-31 related to compounds if limited to invention of Group I, would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second

paragraph and others, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

13. The following is a statement of reasons for the indication of allowable subject matter: The closes prior art reference Brown et al(WO2000018738, also cited as Chemical Abstract DN 132:265091) teaches compounds with a core:"Substituted pyrazine-CH<sub>2</sub>-Phenyl-CO-NH-Phenyl-pyridiene. Sub. Wherein Sub. Is (= -NH-CO-Pyridine".

14. The ref. '738 differs from the instant compounds by not having a core." Pyrazine-NH-CO-NH-Phenyl-Sub. Wherein Sub. Is (= -NH-CO-alkylele-Pyridine or -NH-CO-alkylene-NH-cyclockyl or non-cycloalkyl or -CO-NH-(alkylene)0-1 -pyrrolidine".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is 703 308 4709. The examiner can normally be reached on 6:30 to 5:00 pm. Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on 703 308 4716 or Sr. Examiner Mr. Richard Raymond at 703 308 4523.


The fax phone numbers for the organization where this application or proceeding is assigned are 703 308 4556 for regular communications and 703 308 4556 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.



Sudhaker B. Patel, D.Sc.Tech.  
December 15, 2003.



MUKUND SHAH  
SUPERVISORY PATENT  
EXAMINER  
ART UNIT 1624